Application No.: 09/908,943 Docket No.: 29915/00281A

In the Claims

Claims 1-20 (Withdrawn)

21. (Currently amended) An isolated peptide <u>having 4 to 50 amino acids</u>, <u>said peptide</u> comprising a sequence of at least four amino acids defined by formula P₂P₁₋P₁'P₂', wherein:

P₂ comprises an amino acid selected from the group consisting of N, S, and D;

P₁ comprises an amino acid selected from the group consisting of is Y, L, and Nle;

P₁' comprises an amino acid selected from the group consisting of E, A, and D;

P2' comprises an amino acid selected from the group consisting of A and V; and

wherein a human Aspartyl protease encoded by the nucleic acid sequence of SEQ ID NO: 1 or SEQ ID NO: 3 (Hu-Asp2) cleaves said peptide between P₁ and P₁' =

with the proviso that if P₁'P₂' comprise the sequence DA, P₂P₁ do not comprise the sequences NL or NNIe.

- 22. Cancelled.
- 23. (Original claim) An isolated peptide according to claim 21, wherein the Hu-Asp2 cleaves the peptide at a rate greater than the Hu-Asp2 cleaves a corresponding peptide having the P_2P_1 - P_1 ' P_2 ' amino acid sequence KMDA.
- 24. (Cancelled)
- 25. (Original claim) A peptide according to claim 21, further comprising a label.
- 26. (Currently Amended) A peptide according to claim 21, further comprising a label and a quenching moiety that quenches the label, wherein the label and quenching moiety are attached

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on opposite sides of the P₁₋₋P₁ peptide bind bond, whereby cleavage of the P₁₋₋P₁ peptide bond separates the label and quenching moiety.

- 27. (Currently Amended) A polypeptide comprising:
- a) a peptide sequence having 4 to 50 amino acids, said peptide comprising a sequence of at least four amino acids defined by formula $P_2P_1 P_1'P_2'$, wherein:

P₂ comprises an amino acid selected from the group consisting of N, S, and D;

P₁ comprises an amino acid selected from the group consisting of is Y, L, and NIe;

P₁' comprises an amino acid selected from the group consisting of E, A, and D;

P2' comprises an amino acid selected from the group consisting of A and V; and

wherein a human Aspartyl protease encoded by the nucleic acid sequence of SEQ ID NO: 1 or SEQ ID NO: 3 (Hu-Asp2) cleaves said peptide between P₁ and P₁';

with the provise that if P₁'P₂' comprise the sequence DA, P₂P₁ do not comprise the sequences NL or NNIe; according to claim 21, and

(b) further comprising a transmembrane domain to localize the polypeptide to a cellular membrane when the polypeptide is expressed in a eukaryotic cell.

Claims 28-82 (Withdrawn)

83. (New) An isolated peptide comprising a sequence of at least four amino acids defined by formula P_2P_1 - P_1 ' P_2 ', wherein:

P₂ comprises an amino acid selected from the group consisting of N, S, and D;

P₁ comprises an amino acid selected from the group consisting of is Y, L, and Nle;

P₁' comprises an amino acid selected from the group consisting of E, A, and D;

P2' comprises an amino acid selected from the group consisting of A and V; and

wherein a human Aspartyl protease encoded by the nucleic acid sequence of SEQ ID NO: 1 or SEQ ID NO: 3 (Hu-Asp2) cleaves said peptide between P₁ and P₁';

with the proviso that if P₁'P₂' comprise the sequence DA, P₂P₁ do not comprise the sequences NL or NNIe;

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and wherein said peptide further comprises a detectable label and a quenching moiety, wherein cleavage of the peptide between P1 and P1' separate the quenching moiety from the label to permit detection of the label.

- 84. (New) The isolated peptide according to claim 83, wherein the peptide amino acid sequence consists of 4-50 amino acids.
- 85. (New) The isolated peptide according to claim 83, wherein the Hu-Asp2 cleaves the peptide at a rate greater than the Hu-Asp2 cleaves a corresponding peptide having the P_2P_1 -- P_1 ' P_2 ' amino acid sequence KMDA.
- 86. (New) An isolated peptide having 6 to 50 amino acids, said peptide comprising a sequence of at least six amino acids defined by formula P₃P₂P₁₋₋P₁'P₂'P₃', wherein:

P₃ comprises an amino acid selected from the group consisting of A, V, I, S, H, Y, T and F;

P₂ comprises an amino acid selected from the group consisting of N, S, and D;

P₁ comprises an amino acid selected from the group consisting of is Y, L, and NIe;

P₁' comprises an amino acid selected from the group consisting of E, A, and D;

P2' comprises an amino acid selected from the group consisting of A and V;

P₃' comprises an amino acid selected from the group consisting of E, G, F, H, cysteic acid and S; and

wherein a human Aspartyl protease encoded by the nucleic acid sequence of SEQ ID NO: 1 or SEQ ID NO: 3 (Hu-Asp2) cleaves said peptide between P_1 and P_1' ;

with the proviso that if P₁'P₂' comprise the sequence DA, P₂P₁ do not comprise the sequences NL or NNIe.

87. (New) The isolated peptide of claim 86, wherein said peptide further comprises a detectable label and a quenching moiety, wherein cleavage of the peptide between P1 and P1' separate the quenching moiety from the label to permit detection of the label.

- 88. (New) The isolated peptide according to claim 86, wherein the Hu-Asp2 cleaves the peptide at a rate greater than the Hu-Asp2 cleaves a corresponding peptide having the $P_2P_1-P_1'P_2'$ amino acid sequence KMDA.
- 89. (NEW) An isolated peptide having 4 to 50 amino acids in length comprising a sequence of at least four amino acids defined by formula P₂P₁-P₁'P₂', wherein:

 P_1 is Y;

P₂ comprises an amino acid selected from the group consisting of N, S, and D;

P₁' comprises an amino acid selected from the group consisting of E, A, and D;

P2' comprises an amino acid selected from the group consisting of A and V; and

wherein a human aspartyl protease encoded by the nucleic acid sequence of SEQ ID NO: 1 or SEQ ID NO: 3 (Hu-Asp2) cleaves said peptide between P₁ and P₁'.

- 90. (New) The isolated peptide of claim 89, comprising a sequence of amino acids defined by the formula P₃P₂P₁-P₁'P₂', wherein P₃ comprises an amino acid selected from the group consisting of is selected from the group consisting of I, V and L.
- 91. (New) The isolated peptide of claim 90, comprising a sequence of amino acids defined by the formula P₄P₃P₂P₁-P₁'P₂', wherein P₄ is selected from the group consisting of I, V, and L.
- 92. (New) The isolated peptide of claim 89, wherein said peptide comprises a sequence of $P_3P_2P_1-P_1'P_2'P_3'$, wherein P_3 is I or V, P_1' is E, P_2' is V and P_3' is E.
- 93. (New) The isolated peptide of claim 89, wherein said peptide comprises a sequence of $P_3P_2P_1-P_1'P_2'P_3'$, wherein P_3 is I or V, P_1' is A, P_2' is V and P_3' is E.

- 94. (New) The isolated peptide of claim 89, wherein said peptide comprises a sequence of $P_3P_2P_1-P_1'P_2'P_3'$, wherein P_3 is I or V; P_1' is D, P_2' is V and P_3' is E.
- 95. (New) The isolated peptide of claim 89, wherein said peptide comprises a sequence of P₃P₂P₁-P₁'P₂'P₃', wherein P₃ is I or V; P₁' is D, P₂' is A and P₃' is E.
- 96. (New) The isolated peptide of claim 21, wherein said peptide comprises a sequence of SEISY-EVEFR (SEQ ID NO:152).
- 97. (New) The isolated peptide of claim 21, wherein said peptide comprises a sequence of SEISY-EVEFRWKK (SEQ ID NO:158).
- 98. (New) The isolated peptide of claim 21, wherein said peptide comprises a sequence of SEIDY-EVEFR (SEQ ID NO:153).
- 99. (New) The isolated peptide of claim 21, wherein said peptide comprises a sequence of GLTNIKTEEISEISY-EVEFRWKK (SEQ ID NO:191).
- 100. (New) The isolated peptide of claim 21, wherein said peptide comprises a sequence of TEIDY-EVEFR (SEQ ID NO:151).
- 101. (New) The isolated peptide of claim 21, said peptide comprises a sequence of SEVDY-EVEFR (SEQ ID NO:149).